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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ARIANI, KADE	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
11/29/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,234	YONEHARA ET AL.	
	Examiner	Art Unit	
	KADE ARIANI	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11, 14, and 15* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on December 18, 2009, has been received and entered.

Claims 11, 14 and 15 are pending in this application and were examined on their merits.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/18/2009 has been entered.

Claim Objection

Claim 15 is objected to because of the following informalities:

In claim 15 (page 1 line 1) delete "an amount" and insert –the amount-- in its place.

In claim 15 (page1 line 1) after "a glycated protein" insert –in a sample--.

In claim 15 (page 1 line 5) delete "allowing" and insert –adding a fructosyl amino acid oxidase to react with-- in its place

In claim 15 (page 1 line 6) delete "a fructosyl amino acid oxidase to react with each other".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, and 11, and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 (page 1 line 7 and page 2 line 5) recites the limitation "the redox reaction". There is insufficient antecedent basis for this limitation in the claim, because claim 15 does not recite performing a redox reaction.

In claim 15 (line 4) the recitation "quickly", is indefinite because it fails to set forth the metes and bounds of the instant claim (e.g. how fast the glycated protein must be degraded). The language of a claim must make it clear what subject matter the claim encompasses to adequately delineate its "metes and bounds".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11, 14, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Komori et al. (EP 1 002 874 A2, May 24, 2000) in view of Ledis et al. (US patent No. 5,731,206) and Cosoveanu et al. (Journal of Chromatography A, 1996, Vol. 727, p.324-329) and further in view of Ishimaru et al. (US patent No. 6,127,138)

Claims 11, 14, and 15 are drawn to a method of measuring an amount of a glycated protein, the method comprising, treating a sample containing the glycated protein with a protease in the presence of a sulfonic acid compound and a nitro compound, adding a fructosyl amino acid oxidase to react with a glycated portion of a glycated protein degradation product (obtained by the protease treatment), and measuring the redox reaction, wherein the protease is a metalloproteinase, the redox reaction is measured by determining an amount of hydrogen peroxide generated by the reaction of the glycated portion of the glycated protein degradation product and the fructosyl amino acid oxidase, the amount of the hydrogen peroxide is determined by using an oxidase to reduce the generated hydrogen peroxide and oxidize a substrate that develops color by oxidation and measuring a degree of the color that the substrate

has developed, wherein the degree of the color is measured by measuring an absorbance at a wavelength for detecting the substrate, and the degree of the color is measured by measuring an absorbance at a wavelength for detecting the substrate.

Komori et al. teach a method of measuring the amount of a glycated protein in a sample (measuring glycated proteins in blood, particularly glycated hemoglobin in erythrocytes using a redox reaction) (Abstract, and page 2 0003 and 0004), pre-treating a sample with an oxidizing agent, color-developing tetrazolium compound sodium salt (a nitro and a sulfonic acid compound) (page 2 0010, page 3 0017, page 6 0045, page 7 0061 and 0064, and page 8 0074). It must be noted that a sulfonic acid compound is an organic compound having $HS(=O)_2OH$ formula, and a nitro compound have $-NO_2$ group which may be attached to carbon, nitrogen, or oxygen (see previously cited PAC, Glossary of class names of organic compounds, pages 1369 and 1351). Therefore, the tetrazolium compound of Komori et al. is both a nitro and a sulfonic acid compound. Komori et al. also teach the functional groups, nitro and sulfo, are electron attractive functional groups (page 3 0017). Komori et al. teach the reducing substances in erythrocytes reduce the hydrogen peroxide and inhibit the redox reaction (page 2 0005). Komori et al. teach treating the sample with tetrazolium compound sodium salt which acts as an oxidizing agent not only eliminates the influence of the reducing substances in the sample but also the influence of high molecular weight reducing substances such as proteins (page 2 0011 and page 7 0069 continued on page 8 0070). Komori et al. teach the pretreated sample is treated with a protease (p.6 0050) (treating a sample containing the glycated protein with a protease in the presence of the sulfonic acid

compound and the nitro compound) (page 6 0045, page 7 0061). The decomposed material obtained by the protease treatment is further treated with FAOD (page 6 0053). Komori et al. further teach when the glycated protein in erythrocytes is to be measured whole blood cells or erythrocytes separated from whole blood may be hemolyzed to prepare a sample by conventional method and by using surfactant (page 4 0029 and page 5 0043). Komori et al. further teach degrading the glycated protein by a fructosyl amino oxidase to form hydrogen peroxide and measuring the quantity of hydrogen peroxide formed by measuring the degree of the color (0004, 0030, 0051) using a spectrophotometer (0059), and teach a color-developing substrate and an oxidizing enzyme (a peroxidase) (page 4 0027).

Komori et al. do not teach the sulfonic acid compound and nitro compound is selected form 4-amino-4'-nitrostilbene-2, 2'-disulfonic acid sodium salt, and the protease is a metalloproteinase. However, Ledis et al. teach using benzenesulfonic acid (synonymous 4-amino-4'-nitrostilbene-2, 2'-disulfonic acid, CAS Number: 119-72-2) in a reagent system for selective hemolysis of the erythrocytes (releasing hemoglobin form red blood cells) in a whole blood sample (column 5 lines 46, and 65-66 and column 6 lines 45 and 60). Ledis et al. further teach the suitable sulfonic acid and nitro compound should have electron withdrawing groups (column 6 lines 55-56), and using the reagent in conjunction with sodium salts (column 10 lines 41-46). Therefore, a person of ordinary skill in the art at the time the invention was made would have expected that treating a blood sample in the presence of a nitro and a sulfonic acid compound and a protease would facilitate the release of the glycated protein/glycated hemoglobin form

the erythrocytes and make the glycated hemoglobin more accessible to the degradation by the protease (degradation of the glycated protein would be quicker).

Moreover, Cosoveanu et al. teach 4-amino-4'-nitrostilbene-2, 2'-disulfonic acid sodium salt is a coloring-developing agent (see Introduction 1st column 1st paragraph lines 8-10).

Therefore, in view of the above teachings, a person of ordinary skill in the art at the time the invention was made, recognizing that the reducing substances present in blood may reduce hydrogen peroxide and inhibit the redox reaction, would have been motivated to modify the method as taught by Komori et al. by using a coloring-developing sulfonic acid and nitro compound, 4-aminoazobenzene-4-sulfonic acid sodium salt, according to the teachings of Ledis et al. and Cosoveanu et al. with a reasonable expectation of success in facilitating the degradation of the glycated protein/glycated hemoglobin in a sample containing said glycated protein, an oxidizing agent/a sulfonic acid and nitro compound in the presence of a protease and eliminating the influence of reducing substances, in an attempt to provide a method of measuring the amount of a glycated protein in a sample, because Ledis et al. teach using 4-amino-4'-nitrostilbene-2, 2'-disulfonic acid (a sulfonic and nitro compound and oxidizing agent) for releasing hemoglobin form red blood cells in a blood sample and sodium salts, and because Ledis et al. teach the sulfonic and nitro compounds have electron withdrawing groups (oxidizing agent), and because Komori et al. teach treating the sample with the sulfonic acid and nitro compound and oxidizing agent, tetrazolium compound sodium

salt, eliminates the influence of the reducing substances in the sample and also the influence of high molecular weight reducing substances such as proteins.

Moreover, Ishimaru et al. teach measuring an amount of a glycated protein in a sample by treating the glycated protein with Protease N (a metalloproteinase) (Abstract and Col.11, Table 2) in order to enhance the sensitivity of the detection (Col.5, Lines 59-63). Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to substitute the protease as taught by Ishimaru et al. for the protease in the method of Komori et al. with a reasonable expectation of success in obtaining a glycated protein degradation product, because Ishimaru et al. teach treating the glycated protein with a metalloproteinase to measure an amount of a glycated protein in a sample. The motivation as taught by Ishimaru et al. would be to enhance the sensitivity of the detection. All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. KSR, 550 U.S. at 398, 82 USPQ2d at 1395; Sakraida v. AG Pro, Inc., 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); Anderson 's-Black Rock, Inc. v. Pavement Salvage Co., 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152, 87 USPQ 303, 306 (1950).

Answer to Arguments

Applicant's arguments filed 12/18/2009 have been fully considered but they are not persuasive.

Applicant argues (page 5 2nd paragraph of Remarks filed on 12/18/2010) that Komori indicates that the presence of tetrazole ring as being responsible for the desired effect, therefore one of ordinary skill in the art would clearly understand that their effect is derived from the tetrazolium structure and would not focus on the nitro group, and therefore a person of ordinary skill in the art would not have motivated to substitute one oxidizing agent with another with predictable results.

These arguments are considered and although "the desired effect" stated by Applicant in the arguments is not clear, however the arguments are still not found persuasive, because as mentioned immediately above, Komori et al. teach tetrazole ring of the oxidizing agent and color-developing tetrazolium compound has to be substituted with electron attractive functional groups, selected form nitro and sulfo groups (page 3 0017 and 0018).

In this case, and as mentioned immediately above, a person of ordinary skill in the art at the time the invention was made, recognizing that the reducing substances present in blood may reduce hydrogen peroxide and inhibit the redox reaction, would have been motivated to modify the method as taught by Komori et al. by using a coloring-developing sulfonic acid and nitro compound, 4-aminoazobenzene-4-sulfonic acid sodium salt, with a reasonable expectation of success in facilitating the degradation of the glycated protein/glycated hemoglobin in a sample containing said glycated protein, an oxidizing agent/a sulfonic acid and nitro compound in the presence of a

protease and eliminating the influence of reducing substances, in an attempt to provide a method of measuring the amount of a glycated protein in a sample, because Ledis et al. teach using 4-amino-4'-nitrostilbene-2, 2'-disulfonic acid (a sulfonic and nitro compound and oxidizing agent) for releasing hemoglobin form red blood cells in a blood sample and sodium salts, and because Ledis et al. teach the sulfonic and nitro compounds have electron withdrawing groups (oxidizing agent), and because Komori et al. teach treating the sample with the sulfonic acid and nitro compound and oxidizing agent, tetrazolium compound sodium salt, eliminates the influence of the reducing substances in the sample and also the influence of high molecular weight reducing substances such as proteins.

Moreover, in view of the teachings of Ledis et al., a person of ordinary skill in the art at the time the invention was made would have expected that treating a blood sample in the presence of a nitro and a sulfonic acid compound (oxidizing agent) in the presence of a protease would facilitate the release of the glycated protein/glycated hemoglobin from the erythrocytes and make the glycated hemoglobin more accessible to the degradation by the protease (degradation of the glycated protein would be quicker).

Bauman and Kaminagayoshi references are withdrawn form the rejection therefore Applicant's arguments with respect to Bauman and Kaminagayoshi and the absence of a reason to use a surfactant in the method of Komori are moot.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kade Ariani whose telephone number is (571) 272-6083. The examiner can normally be reached on IFP.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kade Ariani/
Examiner, Art Unit 1651